UNITED STATE DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/492,709	01/27/00	ZYSKIND J	ELITRA.001A

020995 NM12/1023
KNOBBE MARTENS OLSON & BEAR LLP
620 NEWPORT CENTER DRIVE
SIXTEENTH FLOOR
NEWPORT BEACH CA 92660

EXAMINER	
MARSCHEL,A	
ART UNIT	PAPER NUMBER
1631	12

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/492,709	Zyskind et al.
Examiner	**Art Unit**
Ardin Marschel	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on Jul 30, 2001

2a) ☐ This action is **FINAL.** 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) 1-110 is/are pending in the applica

4a) Of the above, claim(s) 1-34, 45-67, 78, 80-84, 94, 95, 97, and 100-110 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) 35-44, 68-77, 79, 85-93, 96, 98, and 99 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) X Claims 1-110 are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ~~X~~ The ~~proposed~~ drawing ~~correction~~ filed on 1/27/00 is: a) X approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) X Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) X Information Disclosure Statement(s) (PTO-1449) ~~Paper No(s).~~ 3 sheets

18) X Interview Summary (PTO-413) Paper No(s) 9

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other

Applicants' election with traverse of Group IX, also electing no specific sequence specie as well as Specie A; claims 35-44, 68-77, 79, 85-93, 96, 98, and 99) in Paper No. 10, filed 7/30/01, is acknowledged. The traversal is directed only to the specie election regarding species A-D and is on the ground(s) that examination of specie A encompasses species B-D. This is not found persuasive because it is well known that there are compounds which directly inhibit a protein polypeptide gene product via active site binding, for example, without antisense type binding reactions being part of the inhibition mechanism, whether at the gene level or during mRNA translation. This species therefore is understood to be directed to such direct polypeptide activity inhibition without being directed to polypeptide amount reduction such as occurs during antisense inhibition, for example. It is also well known that active site inhibition of a protein, for example, is generally published separate from genetic effects such as antisense inhibition thus continuing to document the undue search burden if species A-D were searched together versus A alone. Thus, the above listed claims are under examination as indicated for Specie A as well as considering no specific sequence election.

The requirement is still deemed proper and is therefore made FINAL.

Claims 35-44, 68-77, 79, 85-93, 96, 98, and 99 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35, lines 1-2, indicates that the method is directed to "identifying compounds which reduce the activity of level of a gene product required for cell proliferation". The remainder of the claim then only requires steps for identifying a single compound, albeit with open claim language. Thus, it is unclear whether the practice of a method which only identifies one compound versus identifying multiple compounds defines the metes and bounds of the claim practice. Clarification via clearer claim wording is requested. Claim 85 also contains this unclarity as well as claims dependent directly or indirectly from claims 35 or 85 via said dependence.

Claim 35, lines 1-2, direct the method therein to the identification of compounds which reduce the activity of a gene product required for cell proliferation but then confusingly the claim lacks any step that requires that the gene product is utilized in the cell in a growth rate limiting step. That is, if a compound reduces the activity of a gene product which may be required for cell proliferation but is not a growth rate limiting step material, then reducing its activity in this case will not

inhibit growth but will only reduce the activity of what is already present in an amount beyond its minimal requirement. It is noted that the cell sensitization via antisense nucleic acid is cited in claim 35, lines 3-5, but that this production of a sensitized cell also is not required to obtain a growth rate limiting amount of gene product. Clarification of what criteria actually determines that a compound reduces the activity of a gene product required for cell proliferation when it is not present as a growth limiting rate limiting step is requested to clarify the metes and bounds of what actually is being determined in claim 35. This unclarity due to a lack of defining the claim practice corresponding to or not corresponding to the growth rate limiting step criteria is an issue in all of the instant claims under examination.

Claim 35, last 3 lines, indicates a determination regarding two compared inhibitions but confusingly lacks a conclusion whereby a compound is identified. What criteria is utilized for the identification of the preamble of claim 35? This is an unclarity issue in claims 36-44, 68-77, 79, 85-93, 96, 98, and 99 due to lack preamble correspondence with the actual claim steps. Clarification via clearer claim wording is requested.

In claim 96 the antecedent basis for "said cell" is vague and indefinite in lines 5 in that said cell is contacted with the compound being tested but that this cell already apparently has

been contacted with an agent in line 3. Then in lines 6-8 a comparison between cells some of which have not been provided in earlier steps is performed. Clarification of which said cells are utilized in lines 5 versus the cells in line 7 without agent contact via clearer claim wording.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 35, 36, 44, 85, 86, 96, and 98 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Muller et al. (P/N 5,744,460).

Muller et al. describes the combination therapy of antisense oligonucleotides with chemotherapeutics in the abstract.

Synergistic effects are described for such combinations in the SUMMARY OF THE INVENTION section in column 2. The chemotherapeutics include a broad range of compounds as summarized in column 31, line 51, through column 33, line 59, and are inclusive of protein inhibitors as is the elected subject matter of the instant set of claims. The assessment of antitumor activity for such combinations versus not in combination is exemplified in column 49, line 49, through column 56, line 55, wherein tumor volume, which is deemed to be comparisons of cell proliferation with and without various agents including those as instantly claimed are performed in order to find proliferation inhibitory compounds for use with antisense therapy as also instantly claimed.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the combination therapy evaluation of Muller et al. with and without chemotherapeutics to determine which compound inhibits antisense versus non-antisense treated cells for selection for such combination therapy thus resulting in practicing a specie of the instant invention.

Berlin et al.(P/N 6,277,564) is cited on the enclosed PTO Form 892 as being of interest regarding cellular growth inhibitory substance testing.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 19, 2001

ARDIN H. MARSCHEL
PRIMARY EXAMINER